IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Arnold-Reguigne et al.
Appl. No.: 10/072,900
Conf. No.: 3572
Filed: 12 February 2002
Title: NUCLEIC ACIDS OF THE HUMAN ABCA12 GENE, VECTORS CONTAINING SUCH NUCLEIC ACIDS AND USES THEREOF
Art Unit: 1649
Examiner: Gregory S. Emch
Docket No.: 116696-004

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 CFR 1.132

Sir:

I, Nicolas Duverger, do hereby declare and state:

1. I am familiar with medical genetics, gene mapping and genetic diagnosis.

2. My qualifications in that regard include my being a Senior Research Fellow in human genetics working on functional genomics, I was Head of Tissues and Cell Validation, and was Leader of an ABC binding cassette transporters research program in 2000-2202 with Aventis. My doctoral research related to lipoproteins and I am a reviewer of the Journal of Lipid Research. I am a co-author on publications relating to ABC transporters, and their association with human disease.

3. I read the specification of the above-noted application. The specification clearly conveys to me and I conclude that the inventors possessed a diagnostic assay for medical disorders linked to the ABCA12 gene, such as lamellar ichthyosis.

4.   As known in the art of genetics, a diagnostic assay can be developed if an association between a marker and a disease can be established. The marker need not be located in the gene, the marker can be adjacent to the responsible disease gene. Thus, the predictive power of an assay depends on the degree of correlation of the marker with the pathology, and can range from 100%, a perfect correlation where presence of the marker is always associated with a disease, and lack of the marker is always correlated with lack of the disease, to less than 100% where the presence of the marker almost always, generally and so on is associated with a disease and absence of a marker almost always, generally and so on is associated with absence of the disease. The degree of correlation depends on statistical analyses and relies, in part, for example, on penetrance and sample population size. A diagnostic assay need not and many do not have 100% correlation with a disease.

5.   Gene mapping, whether by cytogenetics or other genetic technique, is known in the genetics and medical genetics arts where diseases are, for example, found to be associated with a particular chromosome, part of a chromosome, or a particular gene or marker.

6.   The above-noted application reported it was known that several medical conditions map to the 2q34 region of human chromosome 2, such as lamellar ichthyosis, see paragraph bridging pages 7 and 8 of the application. Not only are certain diseases mapped to that region of chromosome 2, there are also molecular markers localized to that region, page 8, lines 4-6.

7.   The inventors of the above-noted specification discovered the ABCA12 gene and mapped that gene to the 2q34 region, paragraph bridging pages 8 and 9 of the application.

8.   As noted in the second full paragraph on page 8, the inventors also found different forms of the ABCA12 gene, such as, splice variants and different sized transcripts, and the protein forms were sequenced, see also pages 50-54. Thus, the inventors had markers for the ABCA12 locus, which markers are amenable for use in any of a variety of known diagnostic

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assays, many of which are taught in the application, such as nucleic acid hybridization, see pages 34 and 35, and 54-61 of the application.

9.   Based on that information alone, I conclude that ABCA12 is a marker for lamellar ichthyosis, and thus, can be used in a diagnostic assay for lamellar ichthyosis. That conclusion does not rely on whether ABCA12 is the cause of lamellar ichthyosis. It does mean that ABCA12 is linked to lamellar ichthyosis and thus can be used as a genetic tag for that disease.

10.   The inventors also discovered a preferential expression of the ABCA12 gene in skin and epithelium, a tissue impacted by ichthyosis, page 9, first full paragraph and Example 3.

11.   The application also provides a description of making ABCA12 antibodies, see pages 78-81, using ABCA12 polypeptides made as taught in the application, see pages 77-78 of the application. The ABCA12 antibodies can be used in known immunoassays for diagnosis, see pages 81 and 82.

12.   The identification of the ABCA12 gene, expression of the ABCA12 protein and of variants provides for the development of diagnostic assays for any medical condition linked to the ABCA12 gene, whether, for example, identified by observational correlation, gene mapping and so on.

13.   Therefore, I am convinced on reading of the application noted above that the inventors of the above-noted application were in possession of a diagnostic assay for lamellar ichthyosis using the statistically linked ABCA12 gene, all of which is clearly described in the above-noted application.

15.   Further Declarant sayeth not.

I hereby declare that all statements herein of my knowledge are true; those made on information are believed to be true; and were made with the knowledge that willful false

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statements are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and may jeopardize the validity of any patent that matures from this application.

Dated: _19 Decembre 2006_

Nicolas Duverger